BESTPractices in PRIMARY CARE℠

Lipid Control Today:
Management within the Context of other Cardiovascular Risk Factors

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Best Practices Pearls

- Elevated levels of atherogenic cholesterol – cholesterol carried by apo B-containing lipoprotein particles (non-HDL-C and LDL-C) – is causally related to the development of atherosclerosis
- Dietary advice should focus on lowering bad fats, increasing good fats, and not on dietary cholesterol
- Utilize risk stratification and assessment of other CV risk factors before treating
- Use statins as first line therapy
- The role of 'add-on' therapy, including investigational therapies will continue to evolve
- Guidelines are just that – continue to individualize therapy

2013 ACC/AHA Lipid Guidelines

2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults
A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines
Endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation, American
Pharmacists Association, American Society for Preventive Cardiology, Association of Black
Cardiologists, Preventive Cardiovascular Nurses Association, and WomenHeart: The National Coalition
for Women with Heart Disease

Stone NJ, et al, *Circulation*. 2014;129:S1-S45.

Recommendation 1:
Continue to Focus on TLC

Lifestyle as the Foundation for ASCVD Risk Reduction Efforts

- "It must be emphasized that lifestyle modification (ie, adhering to a heart healthy diet, regular exercise habits, avoidance of tobacco products, and maintenance of a healthy weight) remains a critical component of health promotion and ASCVD risk reduction, both prior to and in concert with the use of cholesterol lowering drug therapies"
- See the 2013 Lifestyle Management Work Group Guideline for lifestyle recommendations for healthy adults[1]

Stone NJ, et al, *Circulation*. 2014;129:S1-S45.
[1] Eckel RH, et al. *Circulation*. 2014;129(25 Suppl 2):S76-99.

TLC, therapeutic lifestyle change
ASCVD, Atherosclerotic Cardiovascular Disease

Recommendation 2:
Use Statins in these 4 Groups Regardless of Lipid Levels

1. Established Atherosclerotic Cardiovascular Disease (ASCVD)
2. Baseline LDL-C at least 190 mg/dl and at least 21 years of age
3. Diabetes and age 40-75 (with LDL-C at least 70 mg/dl)
4. At least 7.5% estimated 10-year ASCVD risk and age 40-75
   - Should start a 'conversation'

Stone NJ, et al, Circulation 2014;129:S1-S45.

Recommendation 3:
Use Only Evidence Based Statin Doses

- Moderate Intensity Statin (daily dose lowers LDL-C by 30%-50%)
  - Age over 75 with ASCVD
  - Diabetes and 10 year ASCVD risk <7.5%
  - Primary prevention with 10 year ASCVD risk at least 7.5% (moderate or high intensity)
  - Not a candidate for high intensity statin
- High Intensity Statin (daily dose lowers LDL-C by at least 50%)
  - Age <75 years and ASCVD
  - Baseline LDL-C > 190 mg/dl
  - Diabetes and 10 year ASCVD risk >7.5%
  - Primary prevention with 10 year ASCVD risk at least 7.5% (moderate or high intensity)

Stone NJ, et al, *Circulation*. 2014;129:S1-S45.

LDL-C – low density lipoprotein concentration

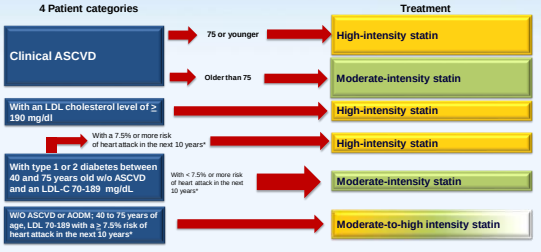
ACC/AHA 2013:
Definition of High, Moderate and Low Intensity Statin Agents and Doses

High-Intensity Statin Therapy	Moderate-Intensity Statin Therapy	Low-Intensity Statin Therapy
Daily dose lowers LDL-C on average, by approximately ≥50%	Daily dose lowers LDL-C on average, by approximately 30 to <50%	Daily dose lowers LDL-C on average, by approximately <30%
Atorvastatin 40*-80* mg Rosuvastatin 20*-40** mg	Atorvastatin 10* (20**) mg Rosuvastatin (5**) 10* mg Simvastatin 20*-40* mg Pravastatin 40* (80**) mg Lovastatin 40* mg Fluvastatin XL 80** mg Fluvastatin 40 mg BID* Pitavastatin 2-4** mg	Simvastatin 10** mg Pravastatin 10*-20* mg Lovastatin 20* mg Fluvastatin 20**-40** mg Pitavastatin 1** mg

*Statins demonstrating reduction in major CVD events
**FDA approved doses not tested in clinical trials*

Stone NJ, et al, *Circulation*. 2014;129:S1-S45.

ACC/AHA 2013
Summary of Statin Treatment Recommendation



Stone NJ, et al, *Circulation*. 2014;129:S1-S45.

Recommendation 4:
Non-statin Medications Not Generally Recommended

- "Because few trials have been performed with non-statin cholesterol-lowering drugs in the statin era, and those that have were unable to demonstrate significant additional ASCVD event reductions in the RCT populations studied, there was less evidence to support the use of non-statin drugs for ASCVD prevention"
  - May be a role in truly statin intolerant or those who achieve a less than adequate therapeutic response

Stone NJ, et al, *Circulation*. 2014;129:S1-S45.

RCT – randomized controlled trial

Recommendation 5:
No LDL or non-HDL Goals

A New Perspective on LDL– C and/or Non-HDL– C Treatment Goals

- The Expert Panel was unable to find RCT evidence to support continued use of specific LDL–C and/or non-HDL–C treatment targets
- The appropriate intensity of statin therapy should be used to reduce ASCVD risk in those most likely to benefit

Stone NJ, et al, *Circulation*. 2014;129:S1-S45.

RCT – randomized controlled trial

Committee's Rationale for Doing Away with Treatment Targets

- The difficulty of giving up the treat-to-goal paradigm was deliberated extensively over a 3-year period
- However, the RCT evidence clearly shows that ASCVD events are reduced by using the maximum tolerated statin intensity in those groups shown to benefit
- After a comprehensive review, no RCTs were identified that titrated drug therapy to specific LDL–C or non-HDL–C goals to improve ASCVD outcomes

Stone NJ, et al, *Circulation*. 2014;129:S1-S45.

RCT – randomized controlled trial

Recommendation 6:
Use New 'Global Risk' Assessment for Primary Prevention

Global Risk Assessment for Primary Prevention

- This guideline recommends use of the new Pooled Cohort Equations to estimate 10-year ASCVD risk in both white and black men and women
- By more accurately identifying higher risk individuals for statin therapy, the guideline focuses statin therapy on those most likely to benefit
- Before initiating statin therapy, this guideline recommends a discussion by clinician and patients

Stone NJ, et al, *Circulation*. 2014;129:S1-S45.
2013 Prevention Guidelines Tools-CV Risk Calculator. http://my.americanheart.org/cvriskcalculator

Committee's Rationale for Using 7.5% Global Risk Cut-off
(As Opposed to Cholesterol Levels)

- The poor discrimination of RCT inclusion criteria for identifying those at increased 10-year ASCVD risk is shown by a calculation performed by the Risk Assessment Work Group using nationally representative data from NHANES
- Use of the RCT inclusion criteria (from RCTs that found a reduction in ASCVD events to guide initiation of statin therapy) would result in:
  - Treatment of 16% of individuals with <2.5% estimated10-year ASCVD risk
  - Treatment of 45% of those with 2.5% to <5% estimated 10-year ASCVD risk (many would say inappropriately)
  - No treatment of 38% of those with ≥7.5% 10-year ASCVD risk would not have been identified as candidates for statin therapy

Stone NJ, et al, *Circulation.* 2014;129:S1-S45.

Recommendation 7:
Consider 'Emerging Risk Factors' In Some Patients

Role of Other Risk Factors, Biomarkers and Noninvasive Tests

- Treatment decisions in selected individuals who are not included in the 4 statin benefit groups may be informed by other factors as recommended by the Risk Assessment Work Group guideline
- Particularly consider in patients with 10 year risk of 5 to <7.5%

Other Risk Factors that May Be Considered
Family history of premature ASCVD
LDL-C > 160 mg/dL
High-sensitivity C-reactive protein ≥2 mg/dl
Coronary calcium score ≥300 Agatston units or ≥75th percentile for age, sex, ethnicity
Ankle-brachial index (ABI) <0.9

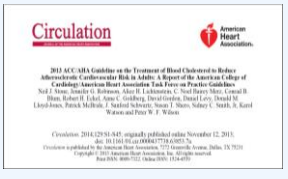
Stone NJ, et al, *Circulation.* 2014;129:S1-S45.

Population Health Aspects of New ACC/AHA Guidelines

- Will lead to more patients treated with statins
- Will likely decrease absolute risk of ASCVD across population (treating more true positives)
- Will increase number of patients taking statins who would never have had a ASCVD event (treating more false positives)
- Will increase number of patients who will not be treated due to guidelines, but will develop ASCVD (treating fewer false negatives)
- Probably a net benefit – but what does this mean for individualized medicine?
- What does this mean for pay-for-performance and the concept of 'control' rates?

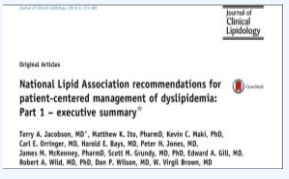
ACC/AHA Guidelines Not the Final or Only Word

Two Different Prevention Approaches - Two Different Complementary Perspectives


Circulation

American Heart Association.

2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines


Journal of Clinical Lipidology

Original Articles

National Lipid Association recommendations for patient-centered management of dyslipidemia: Part 1 – executive summary

Terry A. Jacobson, MD*, Matthew K. Ito, PharmD, Kevin C. Maki, PhD, Carl E. Orringer, MD, Harold E. Bays, MD, Peter H. Jones, MD, James M. McKenney, PharmD, Scott M. Grundy, MD, PhD, Edward A. Gill, MD, Robert A. Wild, MD, PhD, Don P. Wilson, MD, W. Virgil Brown, MD

Stone NJ, et al, *Circulation.* 2014;129:S1-S45.
Jacobson TA, et al. *J Clin Lipidol.* 2014;8:473-488.

'Unifying' Aspects of NLA Recommendations

- Allow for more refined assessment of risk
- Re-introduces goals of therapy
  - Non-HDL-C as the primary target of therapy
- Statin therapy as first line
  - Outlines role of other medications in statin-intolerant or those who do not reach goal

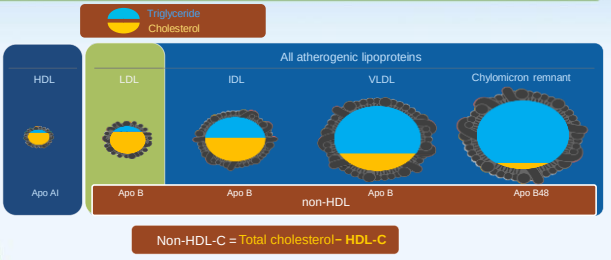
nonHDL-C, non-high density lipoprotein cholesterol concentration

NLA Recommendations
Other Risk Indicators – Consider for 'Refinement' of Risk

1. A severe disturbance in a major ASCVD risk factor
   - Such as multi-pack per day smoking, strong family history, severe hypertension or very low HDL-C
2. Indicators of subclinical atherosclerosis
   - Particularly coronary artery calcium ≥300 Agatston units or ≥75th percentile for age, sex and ethnicity
3. Long-term ASCVD risk ≥40%
   - Lloyd-Jones 2006 Framingham risk calculator (or others)
4. High-sensitivity C-reactive protein ≥2.0 mg/L
5. Advanced Lipid Parameters
   - Apolipoprotein B ≥120 mg/dL
   - LDL particle concentration ≥1600 nmol/L
   - Lipoprotein (a) ≥50 mg/dL (protein) using an isoform insensitive assay
6. Urine albumin / creatinine ratio ≥30 mg/g

Jacobson TA, et al. *J Clin Lipidol.* 2014;8:473-488.

NLA - Focus on Non-HDL-C As Potential Target of Therapy



Jacobson TA, et al. *J Clin Lipidol*. 2014;8:473-488.

NLA Recommendations
Consider Treatment to Specific Goal

Risk Category	Criteria	Treatment Goal Non-HDL-C (LDL-C) (mg/dl)
Low	• 0-1 major RF*	<130 (<100)
Moderate	• At least 2 major RF and 10-year risk <10%*	<130 (<100)
High	• At least 2 major RF and 10-year risk >10% • At least 3 RF • DM with 0-1 other RFs and no end organ damage • CKD stage 3 or 4 • LDL-C >190 mg/dl	<130 (<100)
Very High	• Established ASCVD • DM with at least 2 other RFs or end organ damage	<100 (<70)

*Consider other risk markers
Consider moderate or high intensity statin in patient with ASCVD or DM regardless of baseline lipid levels

Jacobson TA, et al. *J Clin Lipidol*. 2014;8:473-488.

Case 1

- RB is a 57 year-old white man presenting for routine evaluation and care. His cousin, a 58 year old woman had a heart attack recently. He wants to know if he should be doing anything else to decrease his CV risk
- He has no complaints; rides his bike 5 times per week without chest pain or SOB
- PMH notable for hypertension for 4 years
- SH: Smoked for 10 years, but stopped 15 years ago
- FH: Father had an MI at age 72; mother has T2DM
- Medications: Amlodipine 5 mg daily

SOB, shortness of breath; PMH, *past* medical history; SH, social history; FH, family history; T2DM , type 2 diabetes mellitus; MI, myocardial infarction.

Case 1
(continued)

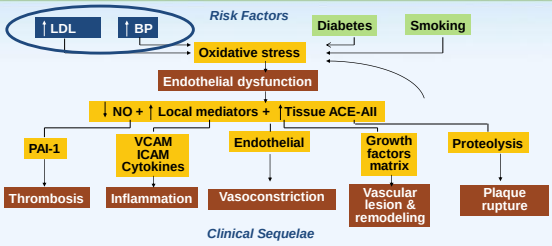
- BP = 142/82 mm Hg
- BMI = 31 kg/m^2, waist circumference = 42”
- Physical examination: unremarkable
- FBS = 108; LFTs normal
- TC = 188; HDL-C = 38; TG = 155; LDL-C = 112 (non-HDL-C = 150 mg/dl)
- ECG: unremarkable
- 10 Year risk of ASCVD (Cohort Equation) = 7.4%
- Lifetime risk of ASCVD (Cohort Equation) = 50%

Recommendation 2:
Use statins in these 4 Groups Regardless of Lipid Levels

1. Established Atherosclerotic Cardiovascular Disease (ASCVD)
2. Baseline LDL-C at least 190 mg/dl
3. Diabetes and age 40-75
4. At least 7.5% estimated 10-year ASCVD risk and age 40-75
   - Should start a ‘conversation’ about risks and benefits
   - Consider emerging risk factors in selected cases, especially if 5%-7.5% risk
   - Important to realize that the calculator is heavily influenced by age

Stone NJ, et al, *J Am Coll Cardiol*. 2014;63(25 Pt B):2889-2934.

Unifying Model of Cardiovascular Risk Factors and Endothelial Dysfunction



Gibbons GH, et al. *N Engl J Med*. 1994;330:1431-1438.

NO, nitric oxide; ACE, angiotensin-converting enzyme; AII, angiotensin II; VCAM, vascular cell adhesion molecule; ICAM, intercellular adhesion molecule

NLA Recommendations
Other Risk Indicators - Consider for 'Refinement' of Risk

1. A severe disturbance in a major ASCVD risk factor
   - Such as multi-pack per day smoking, strong family history, severe hypertension or very low HDL-C
2. Indicators of subclinical atherosclerosis
   - Particularly coronary artery calcium ≥300 Agatston units or ≥75th percentile for age, sex and ethnicity
3. Long-term ASCVD risk ≥40%
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*Consider other risk markers
Consider moderate or high intensity statin in patient with ASCVD or DM regardless of baseline lipid levels

Jacobson TA, et al. *J Clin Lipidol*. 2014;8:473-488.

Case 2

- RS is a 65 year old gentleman with history of non-Q-wave MI 2 years ago – had stent placed at that time
- No recurrent chest pain
- PMH: coronary artery disease, dyslipidemia, hypothyroidism and type 2 diabetes
- Medications: Simvastatin 40 mg daily, aspirin 81 mg daily, metoprolol ER 50 mg daily, losartan 50 mg daily, levothyroxine, metformin 500 mg BID
- SH: quit smoking 2 years ago
- PHYSICAL EXAMINATION:
  - Normal vitals
  - Normal examination

Case 2
(continued)

- Routine lipid panel
  - Total C: 148 mg/dl
  - LDL-C: 66 mg/dl
  - HDL-C: 38 mg/dl
  - Triglycerides: 220 mg/dl
  - Non-HDL-C: 110 mg/dl
- Fasting glucose: 104
- Hemoglobin A1C – 6.6%
- Thyroid Stimulating Hormone (TSH) = 1.3

Recommendation 2:
Use Statins in these 4 Groups Regardless of Lipid Levels

1. Established Atherosclerotic Cardiovascular Disease (ASCVD)
   - High Intensity statin if <75 years of age
2. Baseline LDL-C at least 190 mg/dl
3. Diabetes and age 40-75
4. At least 7.5% estimated 10-year ASCVD risk and age 40-75
   - Should start a 'conversation'

Stone NJ, et al, *J Am Coll Cardiol*. 2014;63(25 Pt B):2889-2934.

ASCVD, atherosclerotic cardiovascular disease

NLA Recommendations
Consider Treatment to Specific Goal

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Improve-It: Study Design

Patients stabilized post ACS ≤ 10 days:
LDL-C 50–125*mg/dL (or 50–100**mg/dL if prior lipid-lowering Rx)
MI (STEMI, 29%; n = 5,192) or UA 24%/non–ST-segment elevation MI 47% (n = 12,952)

↓

Standard Medical & Interventional Therapy

↓

Simvastatin 40 mg | **Ezetimibe / Simvastatin 10 / 40 mg**

↓

Follow-up Visit Day 30, every 4 months

90% power to detect ~9% difference

↓

Duration: Minimum 2 ½-year follow-up (at least 5250 events)

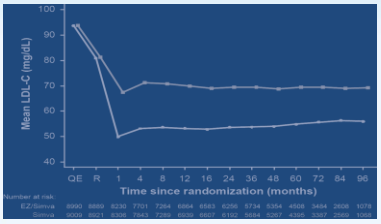
↓

Primary Endpoint: CV death, MI, hospital admission for UA, coronary revascularization (≥ 30 days after randomization), or stroke

N=18,144

Cannon CP. IMPROVE IT Trial, AHA Scientific Sessions 2014; November 15-19, 2014, Chicago Il. Late breaking Clinical Trials LBCT.02.

Improve-It: LDL-C and Lipid Changes



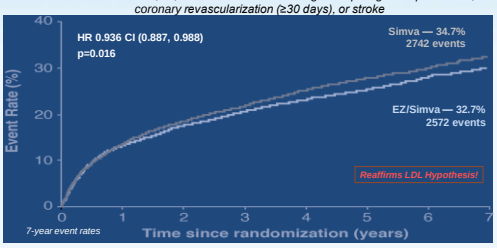
1 Yr Mean	LDL-C	TC	TG	HDL
Simva	**69.9**	145.1	137.1	48.1
EZ/Simva	**53.2**	125.8	120.4	48.7
Δ in mg/dL	-16.7	-19.3	-16.7	+0.6

Median Time avg
69.5 vs. 53.7 mg/dL

Cannon CP. IMPROVE IT Trial, AHA Scientific Sessions 2014; November 15-19, 2014, Chicago Il. Late breaking Clinical Trials LBCT.02.

Improve-IT Primary Endpoint

Cardiovascular death, MI, documented unstable angina requiring rehospitalization, coronary revascularization (≥30 days), or stroke



NNT= 50

Cannon CP. IMPROVE IT Trial, AHA Scientific Sessions 2014; November 15-19, 2014, Chicago Il. Late breaking Clinical Trials LBCT.02.

When to Consider Combinations with Statins
Do We Have Evidence of Reduction in CV Events?

Niacin	No Evidence
Fenofibrate	Only Evidence from Subgroup Analysis (ACCORD LLT)
Fish Oil	No Evidence
Ezetimibe	Good Evidence (IMPROVE-IT)
Colesevelam (and other Bile Acid Resins)	No Evidence

Ongoing Clinical Trials with PCSK9 Inhibitors, CETP Inhibitors, and Prescription Strength Omega 3's

Case 3

- 44 year woman comes to your office for a second opinion about her cholesterol. She has been told that she needs to take a statin, but she does not want to because of what she has heard in the media. Besides she says that she is perfectly healthy and in great shape
- PMH: dyslipidemia
- Medications: OTC fish oil 2000 mg daily only
- SH: works out every day; eats Med style diet. Has never struggled with weight. Non-smoker, rare alcohol
- FH: both her mother and her father and her paternal uncle died in their 50s of MI, but they were smokers and ate a "terrible" diet. She has two siblings that are perfectly healthy with normal cholesterol. She has 2 children whom she says are healthy, but she does not know their cholesterol levels
- PE: Normal vitals. Normal examination

Case 3
(continued)

- Routine lipid panel
  - Total C: 282 mg/dl
  - LDL-C: 206 mg/dl
  - HDL-C: 68 mg/dl
  - Triglyceride: 82 mg/dl
- Fasting glucose: 91
- Thyroid Stimulating Hormone (TSH) = 1.2

What is the mostly likely diagnosis?
How to treat?
What should she tell her kids?

Recommendation 2:
Use Statins in these 4 Groups Regardless of Lipid Levels

1. Established Atherosclerotic Cardiovascular Disease (ASCVD)
2. Baseline LDL-C at least 190 mg/dl
3. Diabetes and age 40-75
4. At least 7.5% estimated 10-year ASCVD risk and age 40-75
   - Should start a 'conversation'

Stone NJ, et al, *J Am Coll Cardiol.* 2014;63(25 Pt B):2889-2934.

Familial Hypercholesterolemia (FH):
Clinically Recognizable Genetic Disorder

- Autosomal dominant inheritance
- Estimates range from 1:200 to 1:500 adults
- Usually due to mutations in LDL receptor gene that lead to decrease clearance of LDL particles from plasma
  - Results in early hypercholesterolemia due to lifelong accumulation of plasma LDL
- Evidence of premature CVD
  - Women with evident CV disease in 50's (mean, untreated)
  - Men with evident CV disease in 40's (mean, untreated)
- Cascade screening of families is essential
- Treatment includes statins, cholesterol absorption inhibitors, nicotinic acid, bile acid sequestrants and apheresis
  - Treat other CV risk factors!

Goldberg AC, et al. *J Clin Lipidol.* 2011;5(3Suppl):S1-S8

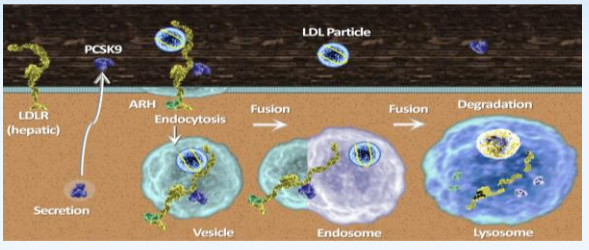
Potential for Investigational PCSK9 Monoclonal Antibodies*

- PCSK9 Binds to the LDL-Receptor (LDL-R) and causes its clearance
  - Up-regulated by statins
- Human population studies
  - Gain-of-function mutation results in hypercholesterolemia
  - Loss-of-function mutation results in low LDL-C and low risk of CV events
- Monoclonal antibodies to PCSK9 in development
  - Significantly reduce LDL-C by approximately 40%-70% in phase 2 and 3 studies
  - Augments statin effect

***Currently Investigational**

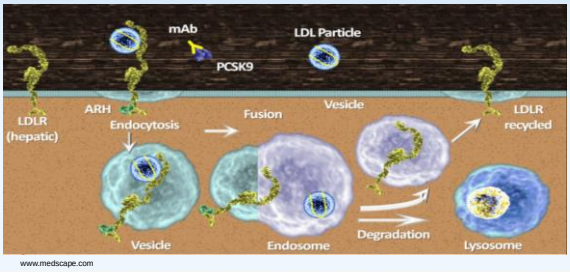
Famier M. *Am J Cardiovasc Drugs.* 2011;11:145-152.

PCSK9 Regulates LDL-R Turnover Through Increased Intracellular Degradation



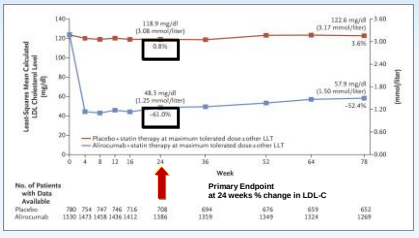
www.medscape.com

Blocking PCSK9 Activity With Monoclonal Antibody Inhibits Intracellular Degradation of LDL-R



www.medscape.com

ODYSSEY LONG TERM Trial



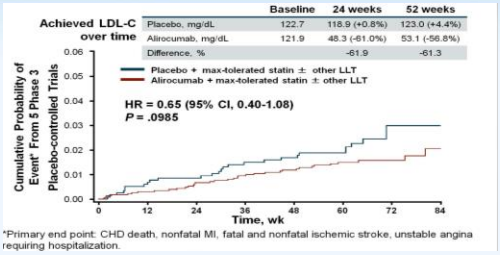
2341 Patients with LDL-C at least 70 mg/dl Despite Maximum Tolerated Statin W or W/O other Lipid-Lowering Drugs Randomized to Alirocumab or Placebo

Post Hoc Analysis:
Major Adverse CV Events
Alirocumab = 1.7%
Placebo = 3.3%
(HR, 0.52, p=0.02)

Alirocumab group had mostly increased risk of
- **Injection site reaction (5.9 vs 4.2%)**
- **Myalgias (5.4 vs 2.9%)**
- **Neurocognitive events (1.2 vs 0.5%)**
- **Ophthalmologic events (2.9 vs 1.9%)**
- **LFT's and CPK no different between groups**

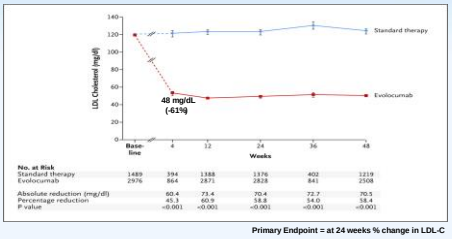
Robinson JG, et al. *N Engl J Med.* 2015;372:1489-1499.

ODDYSSEY Long Term Trial: Post-Hoc Analysis of CV Events



Robinson JG, et al. *N Engl J Med.* 2015;372:1489-1499.

OSLER 1 & 2 Studies



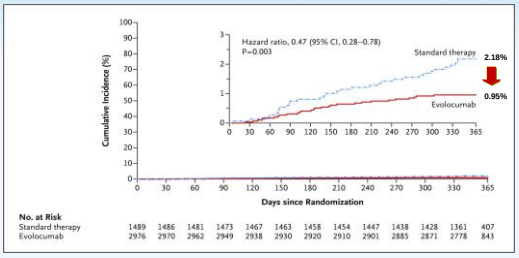
Primary Endpoint = at 24 weeks % change in LDL-C

Long Term Extension Studies Use of Evolocumab Or Standard Therapy (Standard therapy in some cases included statin or ezetimibe)

Adverse Event rates similar in both groups except for neuro-cognitive complaints which were more frequent with evolocumab

Sabatine MS, et al. *N Engl J Med.* 2015;372:1500-1509.

OSLER 1 & 2 Studies
Effect on CV Events (Pre-specified Exploratory Analysis)



Sabatine MS, et al. *N Engl J Med.* 2015;372:1500-1509.

Potential Role for PCSK9 Inhibitors

- Familial Hypercholesterolemia (and other severe dyslipidemias) with statins if tolerated
- Statin Intolerance (with or without low dose statin)
- Addition to statin in high and very high risk individuals (long term outcome studies in progress)

Case 4

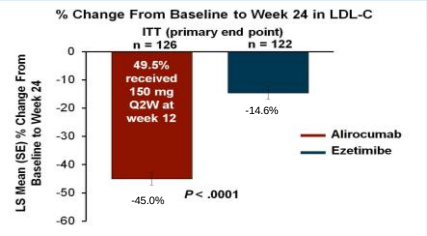
- 62 year old women with type 2 diabetes
- PMH of hypertension, type 2 diabetes, dyslipidemia, hypothyroidism
- Medications include: metformin 500 bid, levothyroxine 0.05 mg, verapamil 180 mg daily, ramipril 10 mg daily, aspirin 81 mg daily
- Started on simvastatin 40 mg daily for LDL-C of 136 mg/dl; HDL = 36 mg/dl
- Within 2 weeks she has bilateral leg and arm pain that is not worsened with ambulation
- Patient heard that statins can cause muscle pain. She stopped statin and her symptoms improved over the next 1-2 weeks
- What should you do?

The Statin "Intolerant" Patient

- LDL-C lowering with statins remains the primary lipid target for most patients to reduce CHD risk
- Options for the patient with myalgias and normal CK
  - Trial of discontinuation for a few weeks and re-challenge
  - Try a lower dose
  - Try a different statin (perhaps with different metabolism or hydrophilicity)
  - Trial of alternate day or weekly dosing (off-label)
  - Check and correct hypothyroidism
  - Check and/or supplement vitamin D
  - Trial of Co-enzyme Q10 (free ubiquinone)
  - Consider non-statin medication (either as mono or combination therapy)

Rosenson RS, et al. *J Clin Lipidol.* 2014;8(3Suppl):S58-S71.

Alirocumab Significantly Reduced LDL-C in Statin Intolerant Patients



Moriarty PM. ODYSSEY Trial, AHA Scientific Sessions 2014; November 15-19, 2014, Chicago Il. Late breaking Clinical Trials LBCT.02.

Best Practices Pearls

- Elevated levels of atherogenic cholesterol – cholesterol carried by apo B-containing lipoprotein particles (non-HDL-C and LDL-C) – is causally related to the development of atherosclerosis
- Dietary advice should focus on lowering bad fats, increasing good fats, and not on dietary cholesterol
- Risk stratify, including assessment of other CV risk factors before treating
- Use statins as first line therapy
- The role of 'add-on' therapy, including investigational therapies will continue to evolve
- Guidelines are just that – continue to individualize therapy

BESTPractices in PRIMARY CARE℠

"This is not the end; it is not even the beginning of the end. But it may, perhaps, be the end of the beginning."

-Winston Churchill